

Oral Medicine and Pathology in 2010

What's Hot
and
What's Not

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Outline (9:00 AM – 10:30 AM)

- Potpourri
 - Xerostomia
 - Candidiasis
 - Bisphosphonates

- BREAK

Outline (10:45 AM – 12:15 PM)

- Recurrent Oral Ulcers
 - Aphthous Ulcers
 - Recurrent Herpetic Infections
 - Lichen planus

- BREAK

Outline (12:30 PM – 2:00 PM)

- Oral Cancer and Related Premalignancy
 - Oral Premalignancy
 - Screening and Diagnostic Tests
 - Oral Cancer

- Q&A

Synopsis

- Major clinical signs and symptoms

- Diagnostic criteria and tests

- Currently accepted therapeutic modalities

References

Iatrogenic Xerostomia

Etiology

- Drug side-effect
- Prescription medications
 - Antidepressants
 - Antihypertensives
 - Psychotherapeutic agents
- OTC medications
 - Antihistamines
- Head and neck radiation therapy

Antidepressants

DRUG	RANK
Prozac® (fluoxetine)	9
Zoloft® (sertraline)	13
Paxil® (paroxetine)	33
Elavil® (amitriptyline)	47
Pamelor® (nortriptyline)	163
Effexor® (venlafaxine)	180

Antihypertensives

DRUG	RANK
Dyazide® (triamterene/HCTZ)	17
Lasix® (furosemide)	23
Esidrix® (hydrochlorothiazide)	94
Tenormin® (atenolol)	116

Psychotherapeutic Agents

DRUG	RANK
Xanax® (alprazolam)	38
Klonopin® (clonazepam)	48
Ativan® (lorazepam)	79
Valium® (diazepam)	133
Restoril® (temazepam)	149



Epidemiology

- One of the most common drug side effects



Clinical Features

- Identical to Sjögren's syndrome
- Temporal relationship to medication use
- Resolution when medication changed or dosage regimen altered



Differential Diagnosis

- Sjögren's syndrome



Diagnosis

- By exclusion



Treatment

- Change medication
- Alter dosage regimen
- Sialogogues
- Artificial saliva



Salivary Stimulants

- OTC sialogogues
 - Sugarless candy
 - Sugarless gum

Treatment

- Water
- Artificial saliva / moisturizers
 - MedOral®
 - Salivart®
 - Oasis®
 - Glandosane®
 - Mouthkote®
 - Oral Balance gel®

Treatment

- Ethyol® (amifostine) – IV before XRT
- Salivary stimulants
 - Salagen® (pilocarpine)
 - Evoxac® (cevimeline)
 - Urecholine® (bethanechol)
- Topical fluoride
 - Prevident® (1.1% neutral NaF)
 - NeutraCare® (1.1% neutral NaF)

Side Effects

- Sweating
- Lacrimation
- Urinary frequency

Dental Caries

- Aggressive therapy
 - Scrupulous oral hygiene
 - Dietary alterations
 - Chlorhexidine mouth rinses
 - Topical fluoride
 - Salivary stimulation

Prognosis

- Variable
- Excellent if medication can be changed or dosage altered
- Poor if permanent damage (radiation)

Candidiasis

Etiology and Epidemiology

- *Candida albicans*
- Most common fungal infection
- 35% of healthy adults
- 90% of denture wearers
- Females > males

Predisposing Factors

- Antibiotics
- Malnutrition
- Xerostomia
- Endocrine dysfunction
 - Diabetes mellitus
 - Pregnancy
 - Oral contraceptives
 - Corticosteroids
- Immunodeficiency
 - Infancy
 - Antimetabolites
 - Acquired

Pseudomembranous Candidiasis

- Infants and debilitated adults
- White, non-adherent plaques
- Erythematous base
- Stomatopyrosis
- stomatodynia

Differential Diagnosis

- Chemical burn
- Allergy
- Hypersensitivity
- Mucous patch
- Morsicatio buccarum / lingualis / labialis

Erythematous candidiasis

- Most common form
- Diffuse erythema
- Variable symptoms
- "denture sore mouth"
 - Limited to denture bearing mucosa
 - Frequently painless

Perlèche

- Angular cheilitis
- Moist, macerated, cracked
- Variable symptoms
- (?) role of decreased vertical dimension
- (?) role of vitamin B complex deficiency

Median Rhomboid Glossitis

- Not a congenital defect
- Posterior dorsal tongue
- Red, depapillated area
- Frequently painless
- Unknown significance

Differential Diagnosis

- Erosive / atrophic lichen planus
- Chemical burn
- Allergy / hypersensitivity
- Impetigo
- Geographic tongue

Diagnosis

- Smear
- Culture
- Biopsy
- Latex agglutination

Treatment

- Topical antifungals
- Systemic antifungals
- Topical antimicrobials

Topical Antifungals

- Nystatin (Mycostatin®)
 - Oral suspension
 - Pastilles
 - Vaginal suppositories
 - Creams and ointments
- Clotrimazole (Mycelex®)
 - Troche
 - Creams and ointments

Systemic Antifungals

- Ketoconazole (Nizoral®)
- Fluconazole (Diflucan®)
- Itraconazole (Sporanox®)

Topical antimicrobials

- Gentian violet
- Chlorhexidine
 - Peridex
 - Periogard

Prognosis

- Excellent prognosis
- Frequent recurrences
- Treat predisposing factors

Bisphosphonates

Textbook Reference

Current Bisphosphonates

- Etidronate (Didronel) – oral or i.v.
- Tiludronate (Skelid) – oral
- Pamidronate (Aredia) – i.v.
- Alendronate (Fosamax; Fosamax plus D) – oral
- Risedronate (Actonel; Actonel with calcium) – oral
- Ibandronate (Boniva) – oral
- Zoledronic acid (Zometa; Reclast) – i.v.

Mechanism of Action

- Inhibits angiogenesis
- Induces tumor apoptosis
- Inhibits osteoclast formation
- Increases osteoclast apoptosis
- Reduce bone resorption/turnover
- **NO BONE REMODELING**

Indications for Use

- Palliation of bone metastasis symptoms
 - Myeloma
 - Breast cancer
 - Prostate
- Treatment of hypercalcemia of malignancy
- Treatment of Paget's disease
- Treatment of avascular bone necrosis
- Prevention & treatment of osteoporosis

Bisphosphonates and Osteonecrosis: In the beginning . . .

- Three case series in 2003-2004
 - Marx (Miami)
 - Migliorati (Ft. Lauderdale)
 - Ruggerio (Long Island)

Marx

- 36 Cases
 - All taking IV pamidronate (Aredia) or Zoledronate (Zometa)
 - Myeloma (n=18)
 - Metastatic breast carcinoma (n=17)
 - Osteoporosis (n=1)
 - 28 cases secondary to tooth extraction
 - 8 cases spontaneous

Migliorati

- 5 cases
 - All taking IV pamidronate (Aredia) or Zoledronate (Zometa)
 - 2 cases following extraction
 - 3 cases spontaneous

Ruggerio, et al.

- 63 cases
 - 56 IV
 - 7 oral (all with osteoporosis)
 - Myeloma (n=28)
 - Metastatic breast carcinoma (n=20)
 - Prostate cancer (n=3)
 - Other malignancies (n=4)
 - 54 cases secondary to tooth extraction
 - 9 cases spontaneous

Current Literature

- Over 500 papers on "osteonecrosis of the jaw" and "bisphosphonate" listed on PubMed
- 60% of papers published since 2003
- 85% concern the association between "osteonecrosis of the jaw" and "bisphosphonate"

Carey JJ and Palomo L. Cleveland Clin J Med 2008;75:871-9

What is the entity known as?

- Bisphosphonate-associated osteonecrosis (BON)
- Osteonecrosis of the jaws (ONJ)
- Bisphosphonate-related osteonecrosis of the jaw (BRONJ)
- Bisphosphonate-induced osteonecrosis of the jaw (BIONJ)
- Bisphosphonate-associated osteonecrosis of the jaw (BONJ).

Incidence

- 0.8% - 1.6% (industry-sponsored)
- 8% - 12% (independent)
- AAOMS
 - 0.01% - 0.04% (oral)
 - 0.8% - 12% (i.v.)

Why are jaws affected and not other bones?

- Jaws have teeth
- Teeth are embedded in bone
- Investing bone has rapid turn over
 - Lamina dura (fastest)
 - Alveolar bone
- Rapidly remodeling bone susceptible to bisphosphonates
- Invasive dental procedures traumatize bone

Why are i.v. bisphosphonates more likely to cause BON?

- Intravenous administration
 - 70% to bone
 - 30% excreted by kidneys
- Oral administration
 - <1% absorbed
 - 0.64% into bloodstream
- 140X increased bone availability with i.v.

Bisphosphonate-associated Osteonecrosis (BON)

- Delayed healing
- Soft tissue breakdown
- Intraoral bone exposure
- ***NO*** decreased vascularity
- Resemble osteopetrosis (Albers-Schonberg or "marble bone" disease)
- Resemble phosphorus poisoning ("phossy jaw")

BON vs. Osteoradionecrosis

- Both have exposed alveolar bone
- BON does ***NOT*** respond to HBO
- BON does ***NOT*** respond to revascularization
- BON affects maxilla ***AND*** mandible

BON Triggers (n=119)

- Spontaneous 25.2%
- Exodontia 37.8%
- Periodontitis 28.6%
- Periodontal sx 11.2%
- Implant 3.4%
- Apicoectomy 0.8%

Marx RE, et al. J Oral Maxillofac Surg 2005;63:1567-75

BON Symptoms (n=119)

- Asymptomatic 31.1%
- Pain 68.9%
- Tooth mobility 23.5%
- Fistula 17.6%

Marx RE, et al. J Oral Maxillofac Surg 2005;63:1567-75

Case Report

- 79 YOWF with non-healing extractions sites (Nos. 20, 21, 22) following "atraumatic" extractions several months previously
- H/O zoledronate (Zometa) for metastatic breast cancer *but not disclosed to DDS or OMS*

JADA, Vol.136:1669 December 2005

Prevention Prior To i.v. Bisphosphonates

- Extract unsalvageable teeth
- Dental prophylaxis
- Treat existing caries
- Treat existing periodontal disease
- Defer bisphosphonates for two months

Prevention During i.v. Bisphosphonates

- Avoid invasive procedures
 - Extractions
 - Periodontal surgery
 - Implant placement
- Treat caries
- Endodontic therapy
- Crown amputation
- Only supragingival scaling
- Splint mobile teeth

Treatment During i.v. Bisphosphonates

- Avoid debridement
- Smooth sharp edges of bone
- Pen-VK, 500 mg, QID
- Chlorhexidine rinses TID
- Flagyl, 500 mg, TID for 10 days (for refractory cases)

Risk versus Benefit

- 1.5 million new fractures annually due to osteoporosis
- 250,000 hip fractures
 - 20% mortality in women
 - 30% mortality in men
 - <25% regain full function

Treatment/Management

- 30 million Rx for bisphosphonates in USA in 2006
- BON will occur in approximately 10% of patients on i.v. bisphosphonates
- BON will occur in <1% of patients on oral bisphosphonates

Principles of Treatment/Management for Patients on Oral Therapy

- No modification of routine treatment
- Regular, routine dental examinations
- Inform patients of risk (<1 in 2,260)
- Good oral hygiene may lower the risk of BON
- There are no validated diagnostic techniques to determine BON risk
- D/C of bisphosphonates may not reduce BON risk

Periodontal Diseases

- Conservative approach may be prudent
- Active infection may exacerbate BON
 - Periapical pathoses
 - Sinus tracts
 - Purulent periodontal pockets
 - Severe periodontitis
 - Active abscesses

Periodontal Diseases

- Non-surgical periodontal therapy, where possible
- No evidence that guided-tissue regeneration or bone grafts increase risk of BON
- Primary closure desirable

Implant Placement and Management

- Minimal data on oral bisphosphonates and implant placements
- Potentially increased risk
 - Multiple implants
 - Guided bone regeneration for ridge augmentation
- Normal implant maintenance
- Non-surgical therapy for peri-implantitis is preferable

Oral and Maxillofacial Surgery

- Small risk for OMFS procedures
- Consider alternative treatment plans
 - Endodontics and crown removal
 - Root exfoliation
 - Bridges and partials rather than implants
- Conservative surgical extractions
 - Primary closure
 - Chlorhexidine rinses
 - Antibiotics only for infection, not prevention

Endodontics

- Endodontics preferable to surgery
- Periapical procedures not recommended
- Endodontic therapy of vital teeth with clinical crown removal and root exfoliation

Restorative Dentistry

- No evidence that malocclusion increases BON risk
- All routine restorative procedures may be done
- Prosthodontic appliances should be evaluated for proper fit

Orthodontics

- Currently no published studies
- Case reports of inhibited tooth movement

Screening Tests

- CTX – measures serum levels of Type I collagen breakdown product (C-terminal cross-linking telopeptide)
- NTX – measures urinary levels of Type I collagen breakdown product (N-terminal cross-linking telopeptide)
- CTX/NTX measures total bone turnover
- Significant age and gender variations in CTX/NTX levels

Screening Tests

- Serum CTX of >150 picograms/ml purported to indicated minimal risk of BON following invasive dental procedures
- Unvalidated recommendation
- Based on uncontrolled, small study (n=30)
- Requires additional data



Prevention of BON

INFORMED CONSENT

BREAK



Aphthous Ulcers



Etiology and Epidemiology

- Immune dysfunction
- Microbial cross-reactivity
- Nutritional deficiency
- Hormonal imbalance
- "Stress"
- Most common oral ulcer
 - 50% of adults in USA affected



Clinical Features

- Never preceded by vesicles
- Only affect non-keratinized mucosa
 - NOT hard palate
 - NOT attached gingiva
- Multiple clinical forms



Minor Aphthous Ulcers

- Most common form
- Small (<1.0 cm)
- Shallow ulcer
- Pseudomembranous covering
- Erythematous halo
- Persist for 7 – 10 days
- Heal without scarring

Major Aphthous Ulcers

- More severe form
- Larger (>1.0 cm)
- Deeper (into muscle)
- Persist for 2-6 weeks
- Heal with scarring

Herpetiform Aphthous Ulcers

- NOT due to infectious agent
- Cluster of multiple small aphthae
- Extremely painful
- Soft palate
- Alveolar mucosa

Behçet's Syndrome

- Oral ulcers
- Ocular ulcers
- Genital ulcers

Differential Diagnosis

- Other viral infections
- Traumatic ulcers
- Pemphigus vulgaris
- Cicatricial pemphigoid
- Other systemic disease

Diagnosis

- History
- Clinical signs and symptoms
- Biopsy ONLY to rule out other entities

Treatment

- OTC medications
- Immunosuppressives
- Occlusive dressings
- Chemical cautery
- Ablation
- Topical antimicrobials
- Thalidomide



Lynch's Law

When in doubt,
treat conservatively



Lynch's Corollary

When something works,
keep using it until it doesn't



Lynch's Paradox

What works for me
may not work for you
and vice versa



Prognosis

- Excellent
- Variable recurrences



Recurrent Herpes Simplex



Etiology and Epidemiology

- Human Herpes Virus 1 (HHV-1)
- #2 most common viral disease
- Majority of individuals in USA exposed
- 50% of individuals give history of contact
- 15% asymptomatic shedders

Clinical Features

- Prodrome
 - Burning
 - Itching
 - Tingling
- Recurrences due to stress
 - Trauma
 - Emotion
 - Endocrine

Clinical Features

- Herpetiform cluster of vesicles
 - Vermilion border
 - Attached gingiva
 - Hard palate
- Infectious for 5-7 days
- Heal in 14 days

Differential Diagnosis

- Impetigo
- Recurrent aphthous ulcers
- Traumatic ulcers
- Other viral stomatitis

Diagnosis


- History
- Clinical signs and symptoms
- Serology
- Viral culture
- Tzanck test

Treatment

- Non-prescription topical antiviral drugs
 - Abreva®
- Prescription topical antiviral drugs
 - Denavir®
- Prescription systemic antiviral drugs
 - Zovirax®
 - Famvir®
 - Valtrex®

Treatment

- OTC remedies
- Iontophoresis
- Do not use corticosteroids



Occupational Hazards



Herpetic whitlow



Herpetic conjunctivitis



Prognosis

- Excellent prognosis
- Variable recurrence pattern



Lichen Planus



Etiology and Epidemiology

- Immunologically-mediated
- Attack basal cells and basement membrane
- Middle age
- Females >> males
- Exacerbated by "stress"

Clinical Features (Skin)

- Scaley, papular, pruritic rash
- Peripheral Wickham's striae
- Arms, thighs, sacrum
- >65% with oral lesions

Clinical Features (Mucosa)

- Widespread involvement
 - 75% buccal mucosa and tongue
 - 20% labial mucosa and gingiva
 - <5% palate and floor of mouth
- <35% with skin lesions
- Multiple clinical forms
 - Reticular/plaque forms - asymptomatic
 - Erosive/atrophic/bullous forms - symptomatic

Differential Diagnosis

- Leukoplakia
- Lupus erythematosus
- Aphthous ulcers
- Pemphigus vulgaris
- Cicatricial pemphigoid
- Erythema multiforme

Diagnosis

- Biopsy is mandatory
- Routine histopathology
- Direct immunofluorescence
 - BMZ fibrinogen to rule out LE

Treatment

- No treatment for asymptomatic cases
- Corticosteroids
- Antimetabolites
- Dapsone
- Cyclosporine
- Occlusive dressings

Prognosis

- Good prognosis
- Moderate morbidity (symptomatic forms)
- Exacerbations and remissions
- (?) premalignant potential
 - <2%
 - Lichenoid dysplasia

BREAK

Oral Cancer and Related Premalignant Lesions

Leukoplakia

- White patch or plaque that cannot be removed or characterized clinically or pathologically as any other disease
- Exclusively *clinical* definition

Etiology

- Tobacco
- Alcohol
- Ultraviolet radiation (lower lip)
- Trauma
- Microorganisms
(*T. pallidum*, *C. albicans*, HPV)
- Idiopathic

Epidemiology

- Most common oral lesion
 - 3% of adults
- Middle-aged and older adults
 - 8% of men over 70
- More common in males (3:1)

Epidemiology

- Dysplasia found in 5-25% of leukoplakias
- Malignant transformation in 4-50% of leukoplakias
 - Average 4%
- Carcinoma *in situ*
 - 2 per 100,000 males
 - 0.5 per 100,000 females

Clinical Features

- 70% involve lips, tongue or gingiva
- Multiple clinical forms
 - Thin
 - Thick
 - Nodular
 - Proliferative verrucous

Tobacco-associated Leukoplakia

- Due to tobacco "tars"
- Usually involve tongue and FOM
- Asymptomatic, well-circumscribed plaque
- Biopsy essential
- Treatment from monitoring to excision
- Fair prognosis

Differential Diagnosis

A list, in decreasing order of probability, of the diseases or conditions that are consistent with the patient's clinical signs and symptoms

Differential Diagnosis

- Morsicatio buccarum
- Leukoedema
- Lichen planus
- Genodermatosis

Diagnostic Methods

Screening and Diagnosis

- History
- Clinical signs and symptoms
- Vital dye (toluidine blue)
- ViziLite® / ViziLite® Plus with TBlue⁶³⁰
- VELScope®
- Identafi®
- Exfoliative cytology
- Brush Test®
- Punch /scalpel biopsy

Oral Cancer Detection

- 80% survival with localized disease
- 20% survival with distant metastasis
- **EARLY DETECTION = BETTER SURVIVAL**
- 50% with metastasis at diagnosis
- 65% with clinical symptoms at diagnosis

Visual Clinical Examination

- High sensitivity
 - detect abnormality with ease
- Low specificity
 - diagnose abnormality with difficulty

Problem

- 15% of patients have mucosal abnormality (Bouquot, 1986)
- 25% of malignant lesions appear benign (Sandler, 1962, 1966)
- 30% of soft tissue lesions are misdiagnosed (Dimitroulis, 1992)

Problem

- Unsure which lesions require testing
- Uncomfortable performing scalpel biopsy
- Patients resist incisional biopsy
- **NOT ALL LEUKOPLAKIAS BIOPSIED**

Leukoplakia / Erythroplakia

- Affect 3% of population
- 4-40% malignant transformation
- Only 25% biopsied
- **ALL LEUKO/ERYTHROPLAKIAS SHOULD BE EVALUATED**

General Dental Practice

- 5-10% with benign-appearing oral lesion
 - 95-98% are truly benign
- Can't biopsy 10% of population to detect <1% of clinically false benign lesions
- **CLINICAL INSPECTION ALONE CANNOT ADEQUATELY DETECT ORAL CANCER**

Sandler (JADA, 1966)

- 118,000 VA patients
- 2,758 with visible mouth lesions
- 592 had cytology and biopsy

- **70** of 287 SCC **THOUGHT BENIGN**
- **20** of 28 CIS **THOUGHT BENIGN**
- **11** of 1,801 (-) cytologies **BECAME MALIGNANT**

Diagnostic Goal

- Decrease false negative clinical findings

- Develop non-intimidating technique
 - practitioners
 - patients

Traditional Cytology

- 300,000 - 500,000 cells per smear

- Less than 0.005% abnormal cells

- Searching for a "needle in a haystack"

- People are not good searchers (proof reading)

Traditional Cytology

- Psychological habituation
 - eye sees abnormality
 - brain imposes expected pattern

- Sensitivity below threshold
 - don't detect abnormal cells

Oral Cytology

- Bigger "haystack"
 - more rapid cell turnover
 - more normal cells; bigger dilution

- Fewer "needles"
 - keratinization
 - decreased availability of abnormal cells

Folsom (Oral Surgery, 1972)

- 158,996 patients screened over 3 years

- 6,897 (4%) had oral lesions

- 148 cancers (2%) among oral lesions

- 41/148 (31%) **FALSE NEGATIVE CYTOLOGY**

Oral Brush Biopsy

Oral CDx TM

- Effective
- Easy to use
- Bridges the gap between visual exam and incisional biopsy
- Helps to determine which lesions merit an incisional biopsy
- ADA Seal of Acceptance

Oral CDx TM

- Optimal sample – full transepithelial sampling
- Optimal search – adaptive, non-algorithmic computing
- Optimal interpretation – oral cytology specialists

Clinical Technique

- May be done by RDH in many states
- No anesthesia necessary
- Identify area to be sampled
- Rotate end/side of brush 5-10 times

Clinical Technique

- Rotate brush on slide to transfer cells
- Apply fixative quickly
- Submit specimen and completed form

Laboratory Technique

- Computer scans slide (400 billion / second)
 - Optimized for Papanicolau-stained oral mucosal cells
 - Looks for several dozen "needles" in "haystack" of 500,000 cells
 - Identifies 200 most atypical cells

Laboratory Technique

- Integrated analysis
 - computer **DOES NOT** replace pathologist
- Pathologist scans slide
 - selects 20 representative atypical cells
 - signs out case

Multicenter U.S. Trial

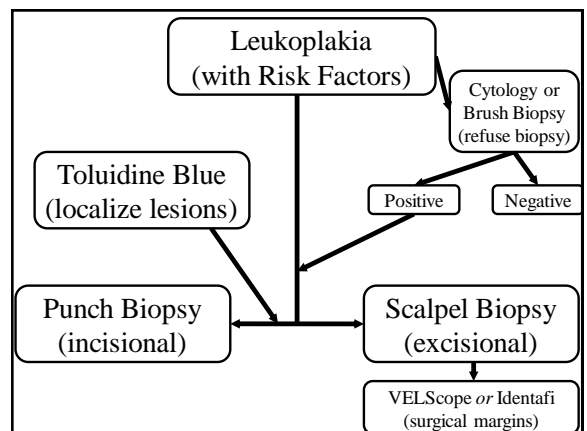
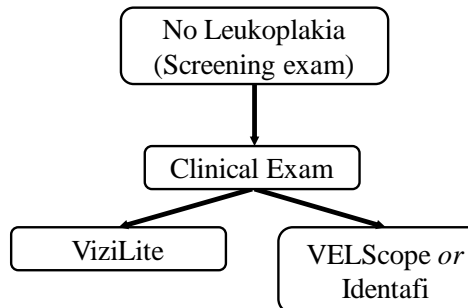
- JADA, October 1999
- 35 academic sites
- 945 patients

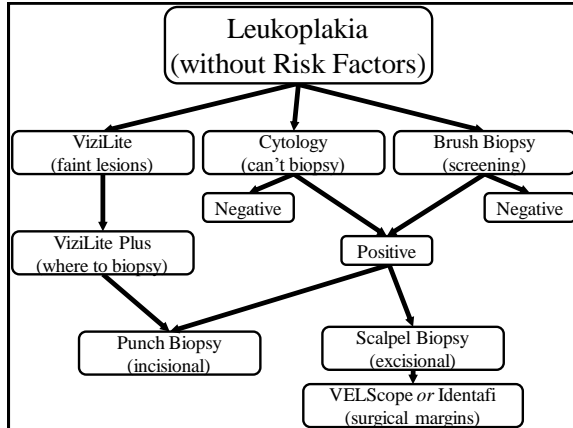
4.5% Dysplasia or Malignancy in Clinically Benign Lesions

BRUSH BIOPSY RESULT	SCALPEL BIOPSY RESULT			
	Malignant or Dysplastic	Benign	Not Done	Total
Positive	14	0	2	16
Atypical	15	0	99	114
Negative	0	0	517	517
Not Done	0	0	0	0
Total	29	0	618	647

Diagnostic Algorithms

- No leukoplakia (clinically normal patient)
- Leukoplakia with risk factors (e.g., tobacco, alcohol, etc.)
- Leukoplakia without risk factors





Treatment

- ~~Nothing~~
- Periodic follow-up
- Excision
- Laser ablation
- Electrosurgery
- Chemotherapy (retinoids)

Prognosis

- Good
- 4% average life-time risk of malignancy
- Malignancies arise 2-4 years later
- Dysplastic lesions more likely to become malignant (10-30%)
- Nodular (10%) and thick (5%) lesions more likely to become malignant

Oral Cancer

Etiology

- Intrinsic factors
 - Nutrition
 - Anemia
 - Immunosuppression
 - Oncogenes

Etiology

- Extrinsic factors
 - Tobacco
 - Alcohol
 - Tobacco AND alcohol (40x risk)
 - Ultraviolet radiation
 - Microbes

Human Papillomaviruses

- **CAUSES** cancer of the
 - Uterine cervix
- **ASSOCIATED WITH** cancer of the
 - Skin Esophagus
 - Vulva Conjunctiva
 - VaginaParanasal sinuses
 - Penis Bronchus

Is HPV Related to H&N Cancer?

- Why suspect HPV?
 - Similar morphologic features between cervical and H&N squamous cell carcinoma
- Why **not** suspect HPV?
 - Detection rate of HPV DNA in H&N squamous cell carcinoma varies from 0-100%.

What Does the Data Show?

- HPV is an **independent** risk factor for oral and oropharyngeal squamous carcinoma
 - 60 studies
 - 5046 patients
 - 25.9% prevalence rate of HPV detection in H&N cancer surgical specimens
 - Higher in oropharyngeal lesions (35.6%) than oral (23.5%) or laryngeal lesions (24.0%)

Which HPV is responsible?

- HPV-16
 - 86.7% of oropharyngeal lesions
 - 68.2% of oral lesions
 - 69.2% of laryngeal lesions

The 64,000 question(s)

- Is there latent HPV that resides in the head and neck?
- If so, where?
- If not, is it transmitted to the head and neck region through sexual contact?

Case-Control Study of HPV and Oropharyngeal Cancer

- 100 patients with new oropharyngeal cancer
- 200 control subjects without cancer
- HPV testing
 - Saline rinse
 - Cytology brush on posterior oropharyngeal wall
 - Serum antibodies (L1, E6, E7)

D'Souza, et al. N Engl J Med 2007;356:1944-56.

Case-Control Study of HPV and Oropharyngeal Cancer

- Significant association with oropharyngeal cancer
 - Oral infection with HPV-16
 - Oral infection with any of 37 other HPV types

D'Souza, et al. N Engl J Med 2007;356:1944-56.

Case-Control Study of HPV and Oropharyngeal Cancer

- HPV-16 found in 72% of paraffin-embedded specimens using *in situ* hybridization (n=60)

D'Souza, et al. N Engl J Med 2007;356:1944-56.

Unhealthy Alcohol Use

Category of Use	Prevalence	Definition and Features
Risky use	30%	>65 years - >7 drinks/week or >3 drinks/occasion <65 years - >14 drinks/week or >4 drinks/occasion
Problem drinking	Varies	Alcohol-related consequences, e.g., "hangover"
Alcohol abuse, harmful use	5%	Failure to fulfill major role obligations; use in hazardous situations; alcohol-related legal problems; social or interpersonal problems
Alcohol dependence, alcoholism	4%	Clinically significant impairment or distress, plus 3 or more of the following: tolerance, withdrawal, excessive time spent obtaining, using or recovering from use, drinking more or longer than intended, inability to control use, continued use despite problems

Saiz R. NEJM 2005;352:596-607

Epidemiology

- 3% of all cancers (#6 in men; #12 in women)
- Increasing incidence beginning in middle age
 - 8 per 100K overall; 30 per 100K after age 75
- 35% associated with pre-existing leukoplakia
- 31,000 new cases annually
- 8,500 deaths annually

Clinical Features

- 90% of cases
 - lower lip
 - ventral tongue
 - floor of mouth
- Most cases present for at least 1 year as an asymptomatic lesion

Clinical Features

- Leukoplakic (white)
- Endophytic (ulcerating)
- Exophytic (fungating)
- Erythroplakic (red)

Differential Diagnosis

- Frictional hyperkeratosis
- Lichen planus
- Traumatic ulcer
- Erythematous candidiasis

Diagnosis

- History
- Clinical signs and symptoms
- Punch biopsy
- Scalpel biopsy

Treatment

- Surgery
- Radiation therapy
- Combination therapy
- Periodic reassessment

Prognosis


- Depends on location and progression
- More anterior location
- No regional lymph node involvement
- No distant metastasis

Grading

- Assessment of biologic behavior based on microscopic features of pleomorphism, cellular maturation, keratin production, etc.
- Grade I – well-differentiated
- Grade II – moderately well-differentiated
- Grade III – moderately differentiated
- Grade IV – poorly differentiated

Staging

- Assessment of survival based on a combination of factors
 - tumor size (T)
 - regional lymph node involvement (N)
 - distant metastasis (M)
- TNM system

 **TNM Staging**

TNM	STAGE	5 YEAR SURVIVAL
T1N0M0	Stage I	85%
T2N0M0	Stage II	66%
T3N0M0 T1-3N1M0	Stage III	41%
Any T4 Any N2-3 Any M1	Stage IV	9%

